A submaximal 1-km treadmill walking test predicts VO_{2peak} in male cardiac patients.

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Outline

- A new test to predict VO_2peak?
- Part I - Development and Validation
- Part II - Prognostic value
- Part III – Clinical application

Part I

- Development
- Validation
- Repeatability

VO_{2peak} predicted *vs* measured

Protocol	n (M/F)	Age (range)	R
Single stage treadmill walking test *	67/72	20 - 59	0.92/0.95
Rockport one-mile walk test *	165/178	30 - 69	0.92/0.93
Cooper Test *	47	17 - 54	0.87
UKK 2-km walking test *	80/79	20 - 65	0.66÷0.76
One-mile treadmill walk test *	154/150	40 - 79	0.87
Six-minutes walking test	198 CHF	26 - 78	0,52

* Subjects with CVD excluded

A new walking test: why?

- VO_2max is a widely considered excellent indicator of cardiorespiratory fitness
  - Diagnostic, prognostic and therapeutic purposes
  - Especially in regard to exercise prescription, either in healthy people (including athletes) and subjects with reduced exercise capacity (including patients).

A new walking test: why?

- Drawbacks of direct assessment that limit its practical application
  - Relatively expensive
  - Time consuming
  - Not well suited for large population
  - Needs maximal or near-maximal effort
  - "Invasive" (mask or mouthpieces)
  - Needs direct medical supervision

A new walking test: why?

- … because of these limitations…
  - Less strenous
  - Less time consuming
  - More cost effective
- …submaximal VO_2peak prediction tests have been developed.

Testing cardiac patients - 1

- The most part of our patients use to walk as training mode.
- Treadmill testing provides a more common form of physiological stress (i.e. walking)
- Ideally a test should allow:
  - Careful monitoring
  - Testing by facilities
  - Short familiarization time
  - No grade
  - Definition of intensity for exercise prescription
  - Completed at low financial and temporal cost

- … the test mode should be consistent with the primary activity used by the participant to address specificity of training issues … (ACSM Guidelines 2005).

Testing cardiac patients - 2

- A test should be:
- Sufficiently "long" to activate cardiorespiratory function.
- Sufficiently "moderate" to avoid the activation of anaerobic glycolysis, in turn reducing risks and bias.

- … an endurance constant work rate protocol … lasting more than 6min … was more sensitive to detect the effects of therapeutic interventions … including cardiopulmonary rehabilitation … (ATS Guidelines 2003).

Testing cardiac patients - 3

- A testing session should be useful to promote and sustain behaviour change
  - to become sufficiently physically active

- … in order to obtain a certain learning effect (i.e. to make experience of moderate intensity)
- … to favor transition from supervised to self-guided exercise program (Wegner et al *Int J Sports Med* 2007).

A new walking test: why?

- … the test mode should be consistent with the primary activity used by the participant to address specificity of training issues … (ACSM Guidelines 2014).

- … an endurance constant work rate protocol … lasting more than 6min … was more sensitive to detect the effects of therapeutic interventions … including cardiopulmonary rehabilitation … (ATS Guidelines 2002).

- … in order to obtain a certain learning trial effect (i.e. to make experience of moderate intensity and to favor transition from supervised to self-guided exercise program (Wegner et al *Int J Sports Med* 2007).

Walking ability

Walking is the second means by which individuals get from place to place in the USA and Europe.	Mitchell C. *Top Geriatr Rehabil*, 2006.
Walking speed is an important predictor of clinical outcomes.	Rabadi MH. *Neurorehabil Neural Repair*, 2005. Ostir GV, et al. *Am J Epidemiol*, 2007. McGinn AP, et al. *Stroke*, 2008. Waite LM, et al. *J Neurol Sci*, 2005.
Walking speed is a 'vital sign' and a surrogate of physiological function.	Cesari M. *JAMA* 2011

Un indice specifico per cardiopatici ?

- L'obiettivo del secondo studio è sviluppare un protocollo per soggetti cardiopatici, sottomassimale, su treadmill, sulla distanza di 1-km, correlato al VO_{2max}

Development Group

anthropometrics

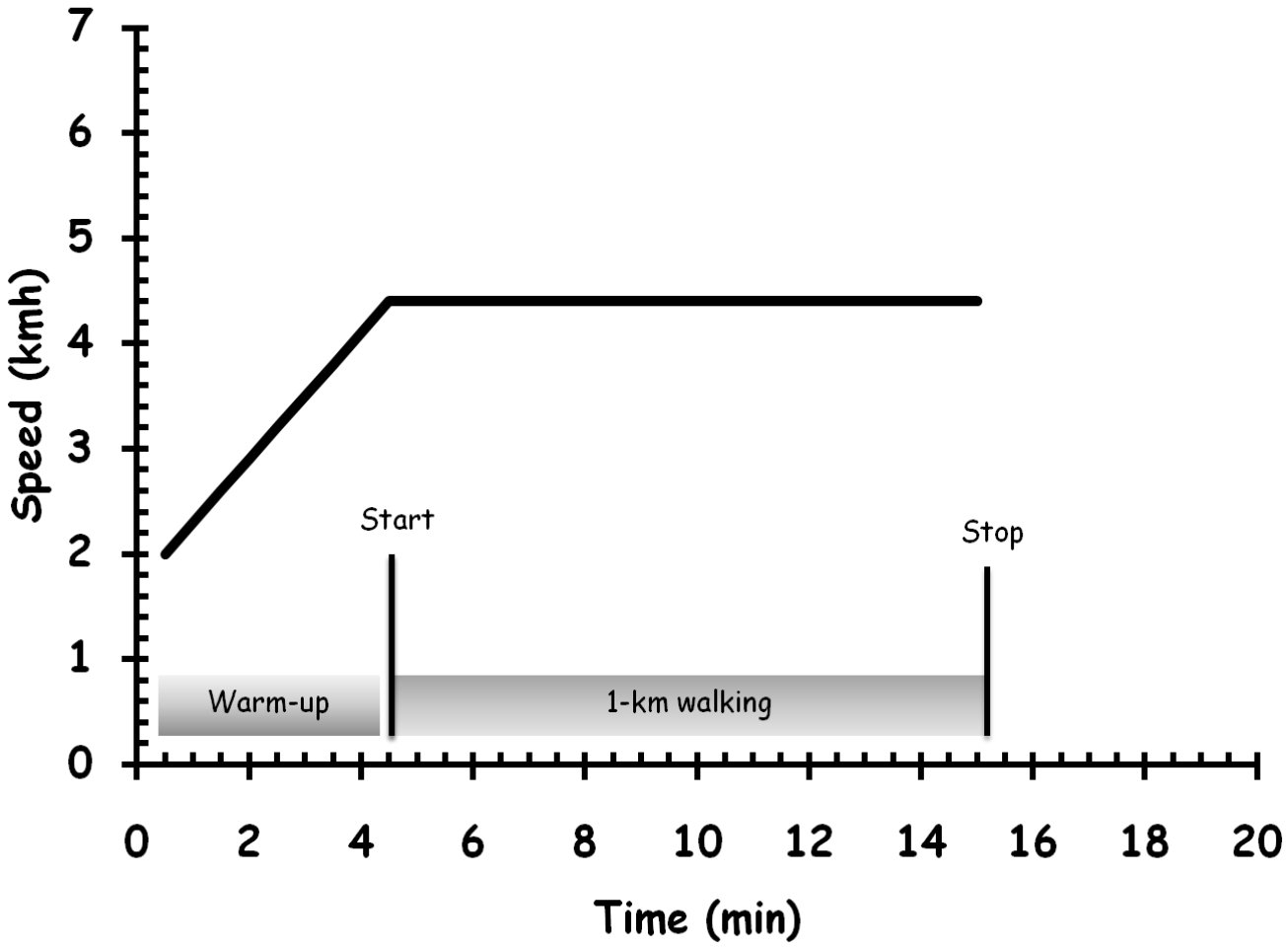
	n = 110
Age (yr)	65 ± 10
Height (cm)	172 ± 6
Weight (kg)	83.5 ± 12
BMI	28 ± 4

Development Group

clinical characteristics

	n = 110
AMI (%)	7
AMI + PTCA or CABG (%)	44
PTCA or CABG, no AMI (%)	37
Other cardiac surgery (%)	16
BB/NBB (n)	41/32
EF (%)	56 ± 9
Weekly physical activity (kcal, Median) (range interquartile)	1100 (800-2150)

1KTWT


Speed (kmh)
0
1
2
3
4
5
6
7
Start
Stop
Warm-up
1-km walking
0
2
4
6
8
10
12
14
16
18
20
Time (min)

Exercise protocol – (1)
1-km treadmill walking test (1KTWT)

- Patients encouraged to walk freely, using handrails for balance only when necessary (*)
- Quickly adaptation when instructed (*)
- Moderate intensity (RPE 11-13/20)
- Grade 0%
- Supervised

- Time/speed
- HR (mean and max)
- Age
- Height
- Weight
- BMI

(*) AACVPR 2004, page 80

Exercise protocol – (2) VO_{2peak} determination

Stage	Duration (min)	Speed (kmh)	Grade (%)
1	1	2.3	1
2	1	2.6	2
3	1	2.9	3
4	1	3.2	4
5	1	3.5	5
6	1	3.9	6
7	1	4.2	7
8	1	4.5	8
9	1	4.8	9
10	1	5.1	10
11	1	5.5	11
12	1	5.8	12
13	1	6.1	13
14	1	6.4	14
15	1	6.8	15
16	1	7.1	16

2004, AACVPR Guidelines for Cardiac Rehabilitation and Secondary Prevention

Test massimale

- almeno 3 dei seguenti criteri
  - RER ≥ 1,05;
  - FC ≥ 85% di FCMT o FCmax ≥ FCMT - 15bpm;
  - RPE ≥ 18/20 della scala di Borg;
  - Tendenza a *plateau* del VO2.

Test incrementale

	NBB	BB
	Media (DS)	**Media (DS)**
VO_{2max} (ml/min)	2058 (535)	2048 (469)
VO_{2max}(ml/min/Kg)	26.0 (7.0)	24 (5)
FC_{max}	142 (18)	131 (23)
RER_{max}	1,08 (0,07)	1,04 (0,07)
Velocità (Km/h)	6,0 (0,9)	6,02 (0,8)
Pendenza (%)	13 (3)	13 (3)
%FCMT	92 (10)	85 (14)

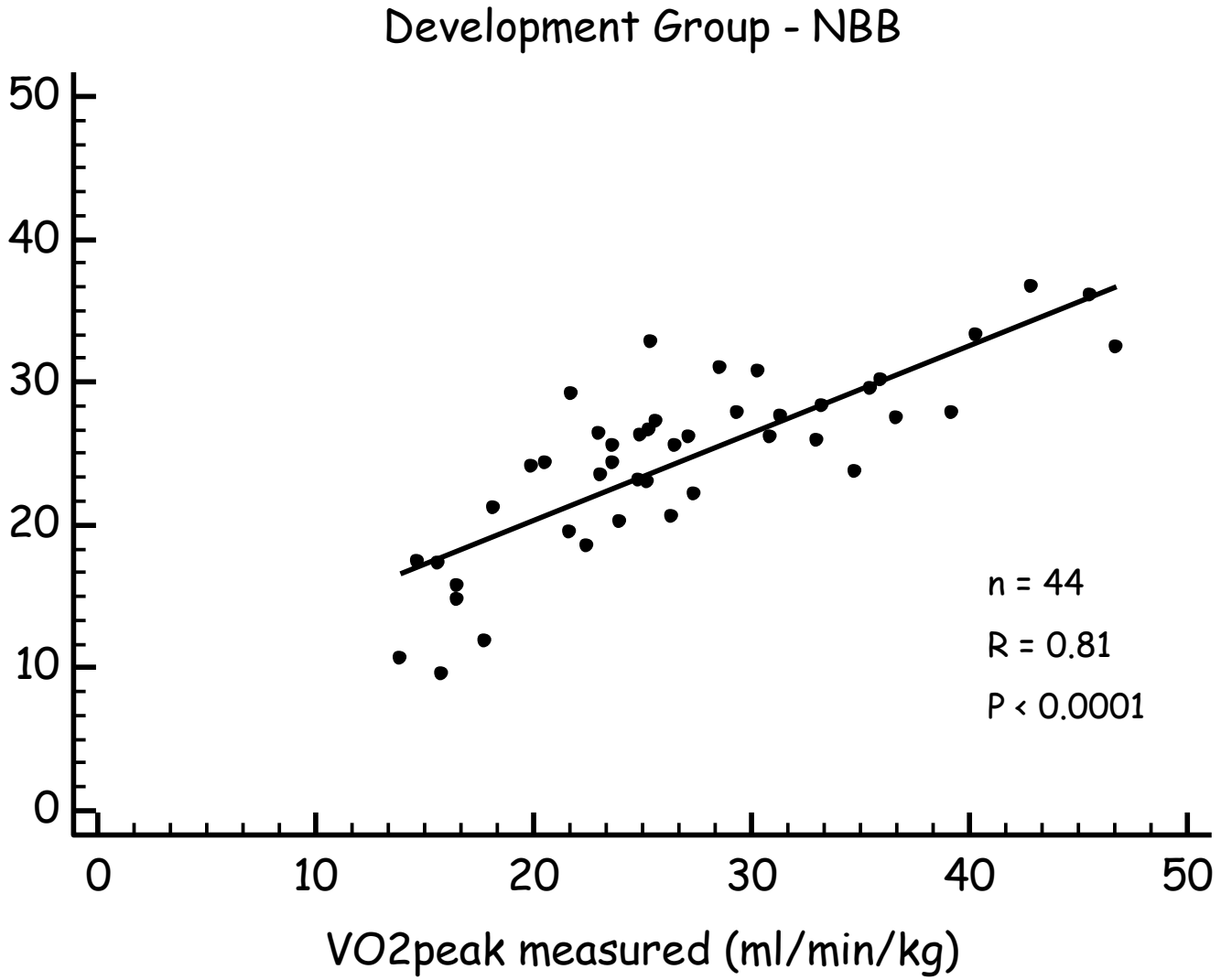
1KTWT

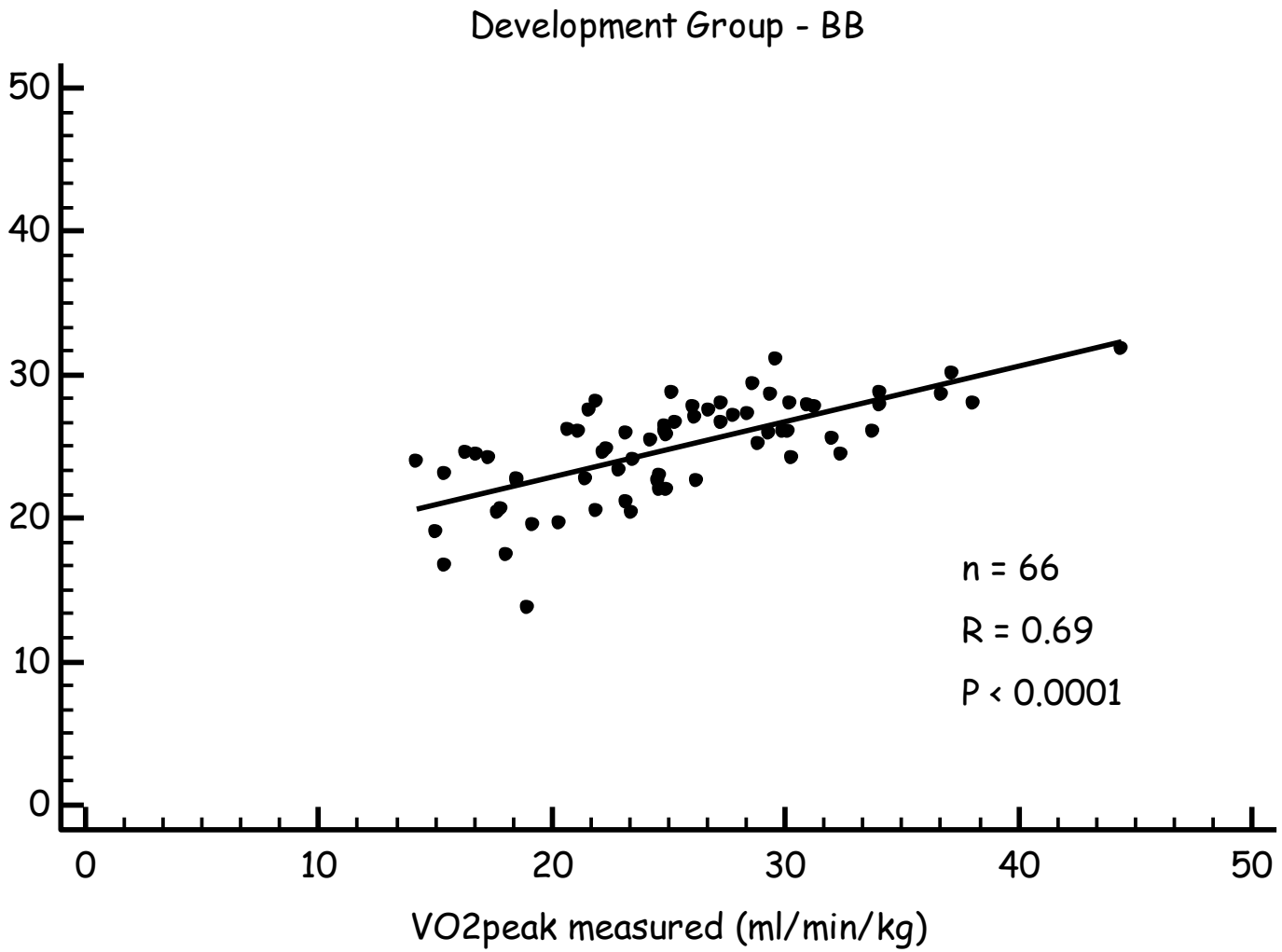
	NBB	BB
	Media (DS)	Media (DS)
tempo	11'22" (2'13")	11'40" (2'33")
FC media (bpm)	105 (13)	97 (14)
FC max (bpm)	117 (18)	106 (16)
RPE	12 (2)	12 (1)
%FCMT	68 (8)	63 (9)
Velocità (Km/h)	5,3 (1,0)	5,2 (0,9)

Predictive Equations

- NBB
  - 46.11 + (4.41 x mean speed) – (0.40 x BMI) – (0.30 x age) – (0.11 x HRmax)
- BB
  - 33.42 + (2.79 x mean speed) - (0.49 x BMI) – (0.14 x age)

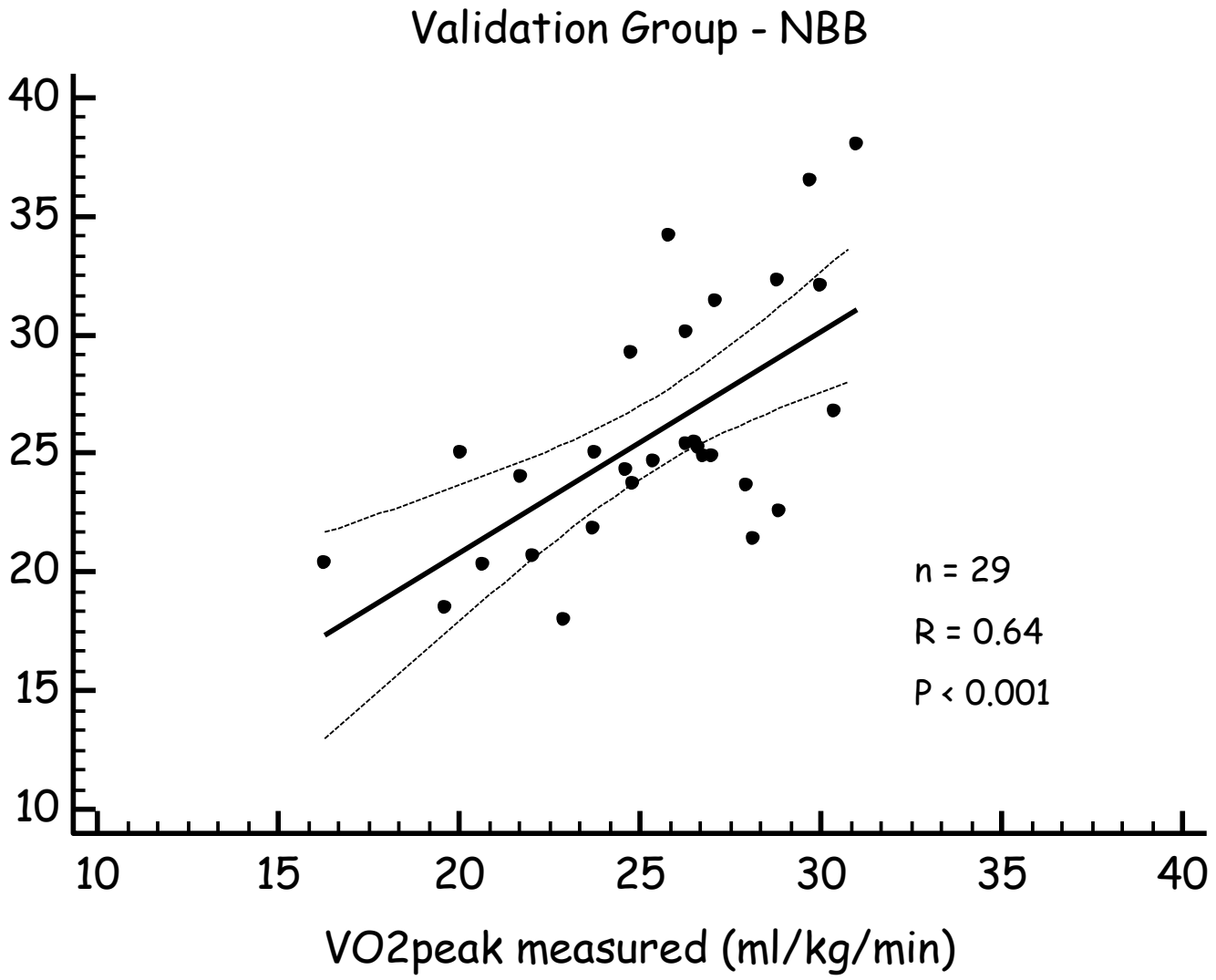
Results

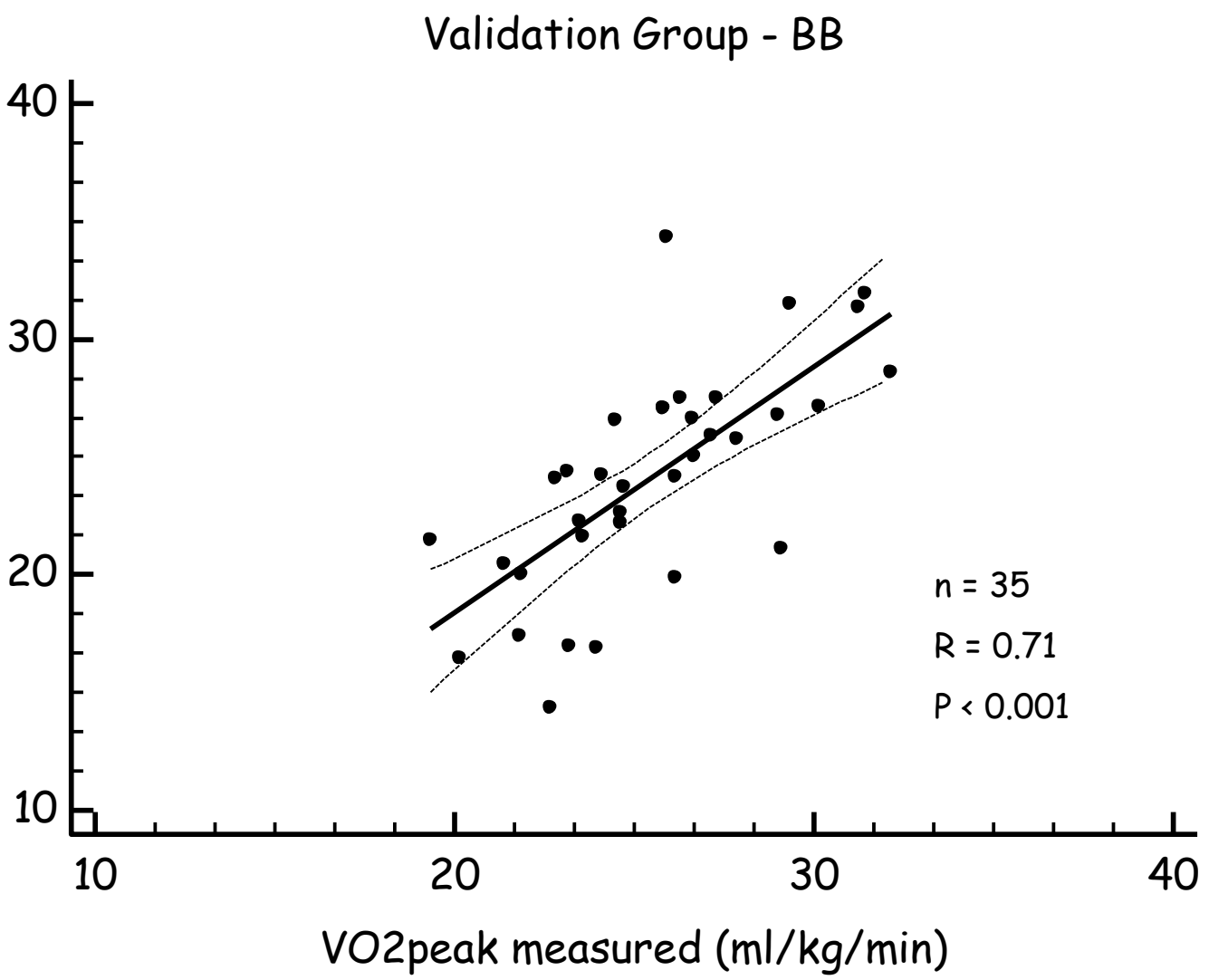

Development Group - NBB
50
40
30
20
10
0
0
10
20
30
40
50
n = 44
R = 0.81
P < 0.0001
VO2peak measured (ml/min/kg)

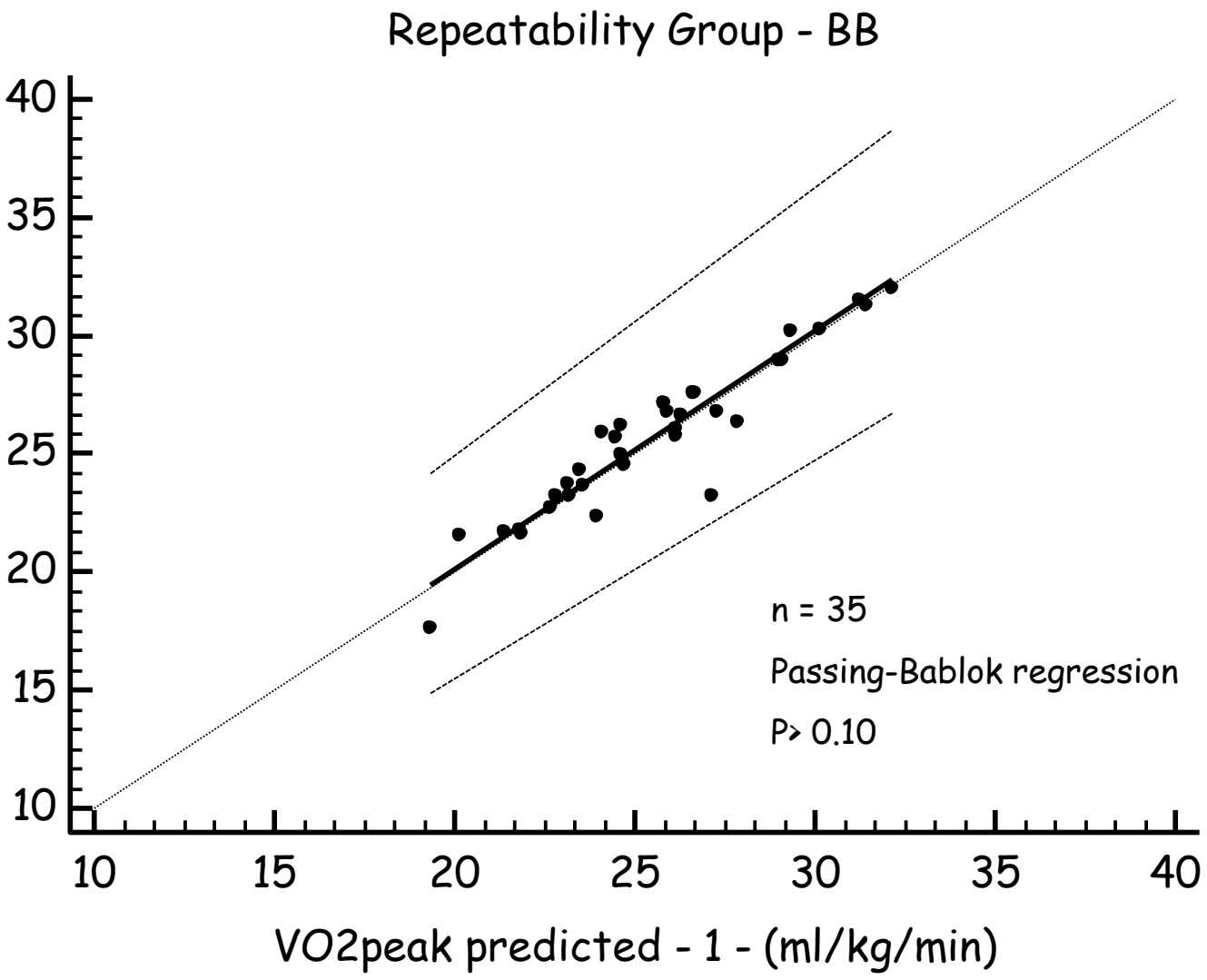

Development Group - BB
50
40
30
20
10
0
0
10
20
30
40
50
n = 66
R = 0.69
P < 0.0001
VO2peak measured (ml/min/kg)

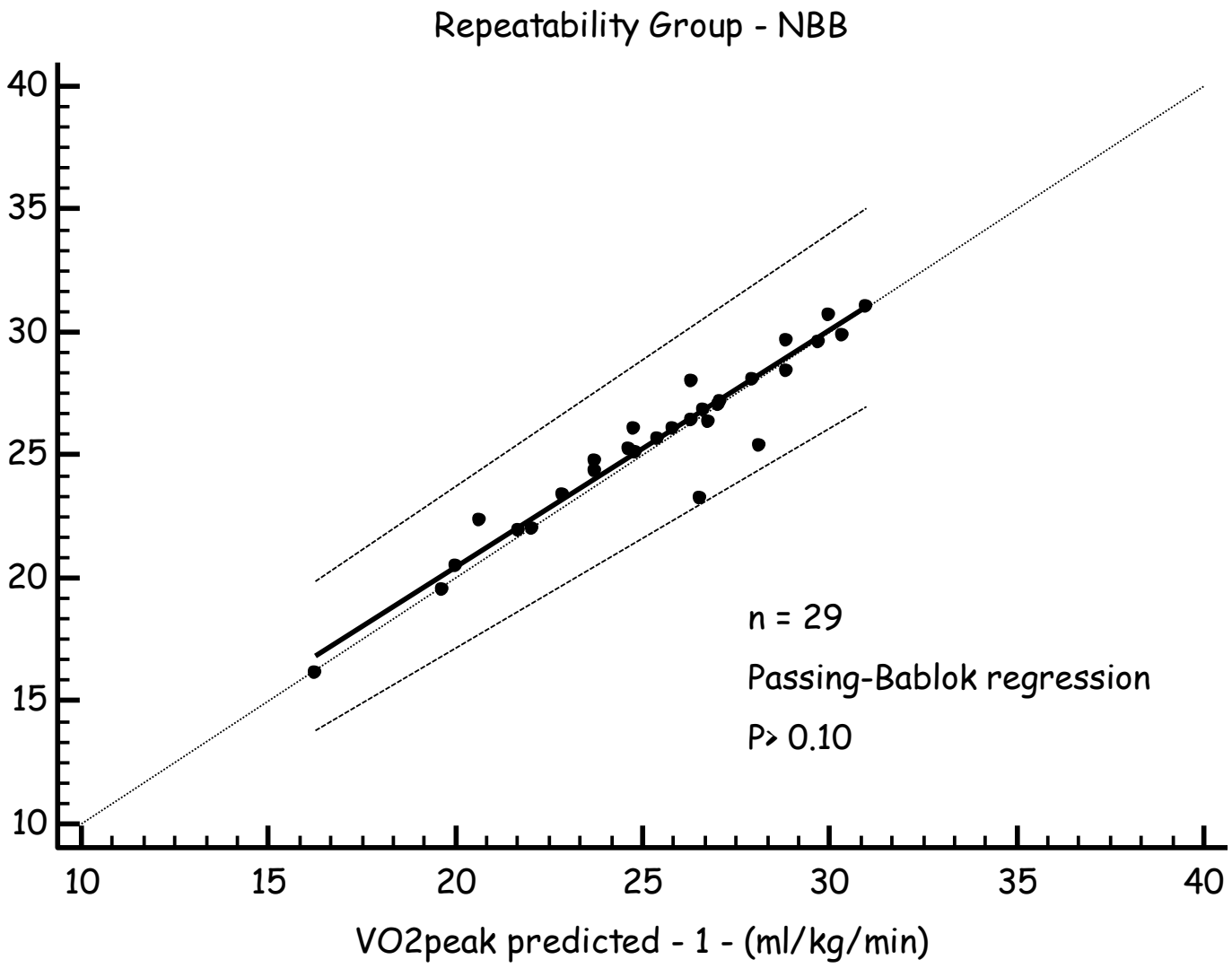
Cross Validation and Repeatability Group

- n = 64
- BB/NBB (35/29)
- Similar characteristics


Validation Group - NBB
40
35
30
25
20
15
10
10
15
20
25
30
35
40
VO2peak measured (ml/kg/min)
n = 29
R = 0.64
P < 0.001


Validation Group - BB
40
30
20
10
10
20
30
40
VO2peak measured (ml/kg/min)
n = 35
R = 0.71
P < 0.001


Repeatability Group - BB
40
35
30
25
20
15
10
10
15
20
25
30
35
40
n = 35
Passing-Bablok regression
P> 0.10
VO2peak predicted - 1 - (ml/kg/min)


Repeatability Group - NBB
40
35
30
25
20
15
10
10
15
20
25
30
35
40
n = 29
Passing-Bablok regression
P> 0.10
VO2peak predicted - 1 - (ml/kg/min)

Conclusioni

- Il VO_{2max} predetto con il "nuovo" algoritmo è positivamente correlato con il VO_{2max} misurato.

Part II

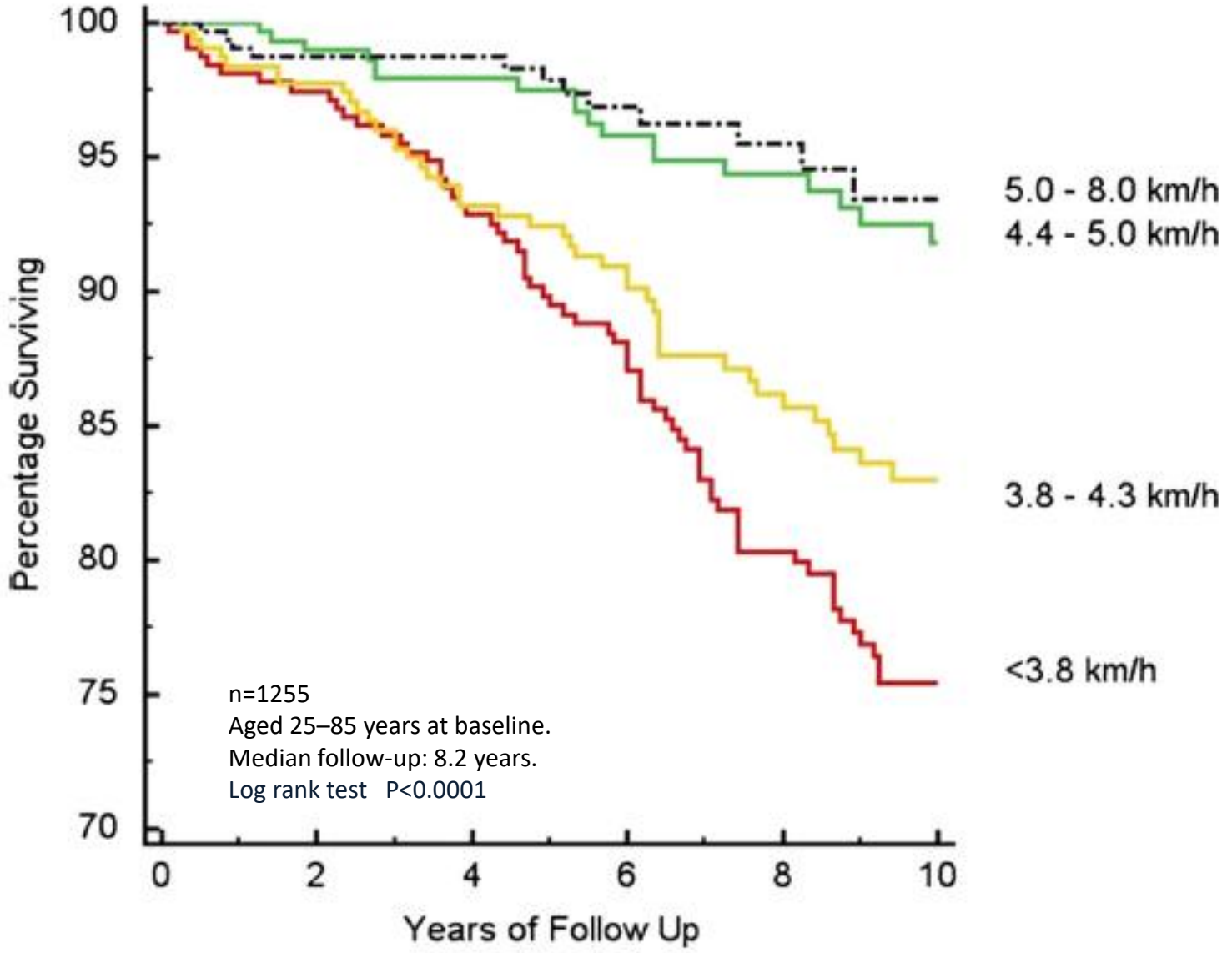
- Validazione prognostica del protocollo
  - Sopravvivenza
  - Ospedalizzazione
  - Analisi dei costi

BMJ Open

Treadmill walking speed and survival prediction in men with cardiovascular disease: a 10-year follow-up study

Chiaranda G. et al *BMJ Open,* 2013.

Walking speed and survival



Chiaranda G. et al *BMJ Open,* 2013.

Table 1 Baseline characteristics of the 1255 participants by quartile of average walking speed

Variable	All Participants (n=1255)	I Quartile (n=316)	II Quartile (n=313)	III Quartile (n=300)	IV Quartile (=326)	p for trend
AWS						
(km/h)	4.3 (0.8)	3.4 (0.3)	4.1 (0.1)	4.6 (0.2)	5.5 (0.5)	<0.001
(m/s)	1.19 (0.22)	0.94 (0.08)	1.13 (0.02)	1.27 (0.05)	1.53 (0.14)	
Deaths (n)	141	68	43	18	12	<0.001
Age (year)	61 (10)	65 (9)	63 (9)	59 (9)	57 (9)	<0.001
Risk factor						
BMI	27.6 (3.4)	28.3 (3.7)	27.6 (3.3)	27.7 (3.2)	27.0 (3.3)	<0.001
LV ejection fraction (%)	56 (10)	53 (11)	56 (9)	57 (11)	58 (10)	0.002
Family history (%)	53.7	48.4	51.7	54.3	60.7	0.001
Fasting glucose (mg/dL)	107 (27)	110 (28)	110 (28)	106 (29)	105 (28)	0.03
Total cholesterol (mg/dL)	194 (42)	195 (47)	199 (43)	194 (41)	188 (39)	0.04
HDL cholesterol (mg/dL)	49 (14)	50 (16)	49 (13)	47 (14)	50 (13)	0.55
Serum triglycerides (mg/dL)	139 (80)	147 (97)	138 (71)	143 (80)	129 (67)	0.046
Serum creatinine (mg/dL)	1.1 (0.2)	1.2 (0.3)	1.1 (0.2)	1.1 (0.2)	1.0 (0.2)	<0.001
Medical history (%)						
CABG	49.4	63.3	52.0	46.3	36.2	<0.001
Myocardial infarction	28.1	22.2	29.1	31.3	30.0	0.02
PTCA	8.7	4.7	5.7	9.0	15.3	0.001
Valvular replacement	8.9	8.2	8.9	7.6	10.4	0.4
Other	4.4	1.3	3.8	5	7.4	0.001
Medications (%)						
ACE inhibitor or ARB	53.3	57.3	54.0	50.0	68.9	0.09
Aspirin	74.6	75.9	72.8	74.3	75.1	0.9
β-Blocker	59.4	57.9	63.6	60.0	55.8	0.4
Calcium antagonist	12.9	13.6	12.5	14.0	11.7	0.6
Diuretic	18.1	26.6	20.4	13.7	10.4	<0.001
Statin	52.9	50.3	49.2	52.0	60.1	0.01
Number of medications	3.2	3.5	3.2	3.1	3.1	0.004

Data are presented as mean (SD).
ARB, angiotensin receptor blocker; AWS, average walking speed; BMI, body mass index; CABG, coronary artery bypass graft; HDL, high-density lipoprotein; LV, left ventricular; PTCA, percutaneous transluminal coronary angioplasty, stenting or both.

AWS quartile	AWS (km/h)	HR	95% CI	P Value
I	3.4 (0.3)	1.00	-	-
II	4.1 (0.1)	0.77	0.52 - 1.13	0.18
III	4.6 (0.2)	**0.41**	0.24 - 0.70	0.01
IV	5.5 (0.5)	**0.36**	0.19 - 0.68	0.002

Full-adjusted relative risk of death from any cause according to quartiles of walking speed

Chiaranda G. et al *BMJ Open,* 2013.

AWS quartile	AWS (km/h)	HR	95% CI	P Value
I	3.4 (0.3)	1.00	-	-
II	4.1 (0.1)	0.77	0.52 - 1.13	0.18
III	4.6 (0.2)	0.41	0.24 - 0.70	0.01
IV	5.5 (0.5)	0.36	0.19 - 0.68	0.002
Each 1 km/h increase		**0,46**		**<0,0001**

Chiaranda G. et al *BMJ Open,* 2013.

International Journal of Cardiology 173 (2014) 248–252

Contents lists available at ScienceDirect

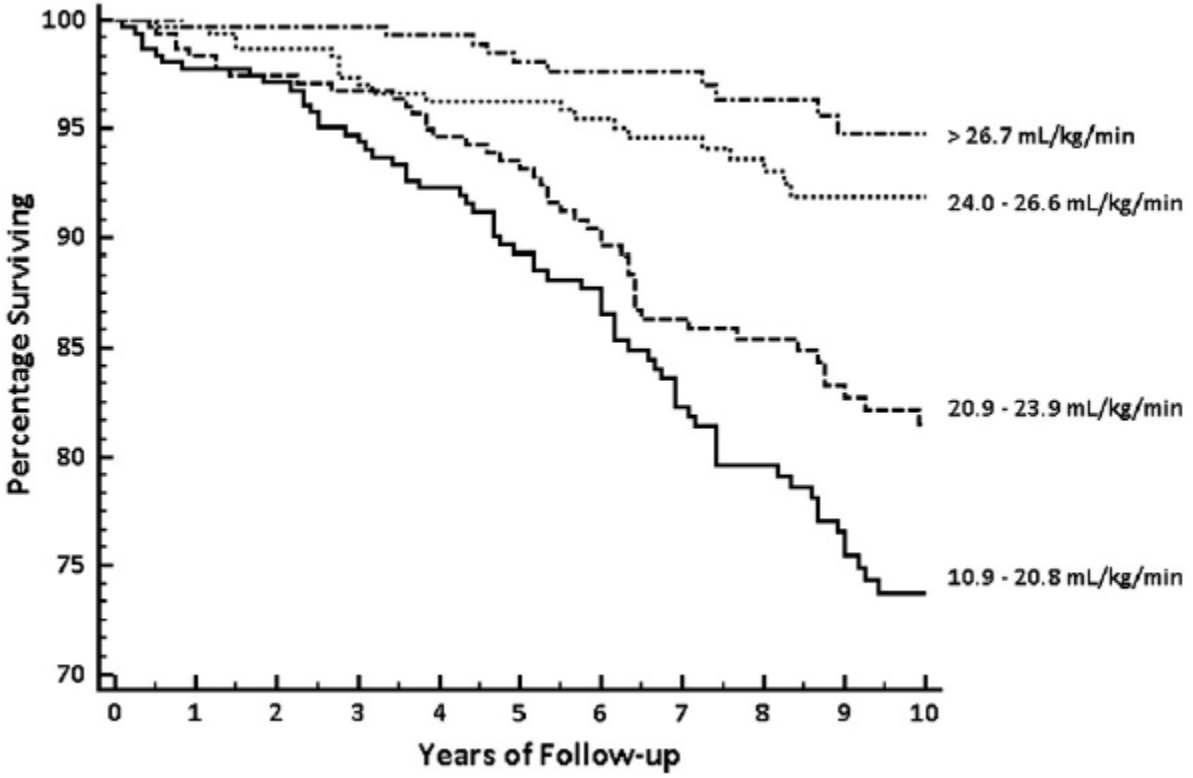
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

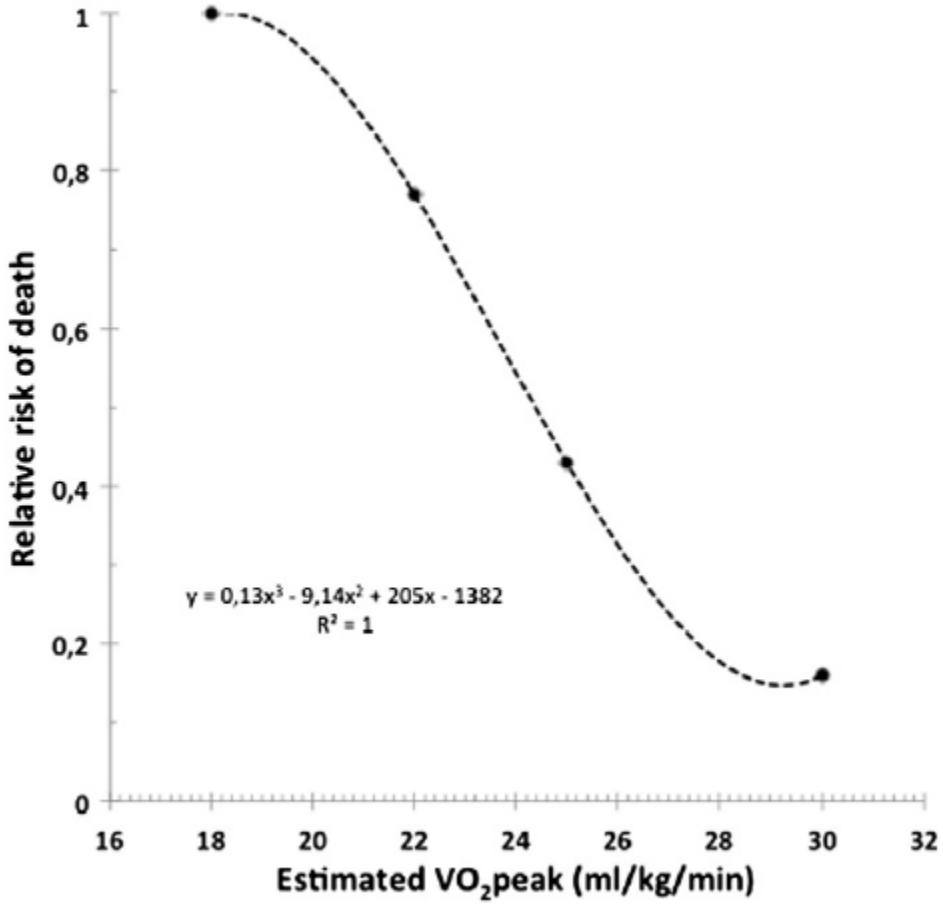
Association between VO_2 peak estimated by a 1-km treadmill walk and mortality. A 10-year follow-up study in patients with cardiovascular disease

Giovanni Grazzi [a], Jonathan Myers [b], Eva Bernardi [a,*], Francesco Terranova [a], Giulio Grossi [a], Luciano Codecà [a], Stefano Volpato [c], Francesco Conconi [a], Gianni Mazzoni [a], Giorgio Chiaranda [a]

Grazzi G. et al. *Int J Cardiol* 2014



Grazzi G. et al. *Int J Cardiol* 2014



Grazzi G. et al. *Int J Cardiol* 2014

VO_2peak Quartile	HR	95% CI	P Value
I	1.00	-	-
II	0.85	0.58 - 1.26	NS
III	**0.50**	0.29 - 0.88	0.02
IV	**0.33**	0.16 - 0.69	0.004

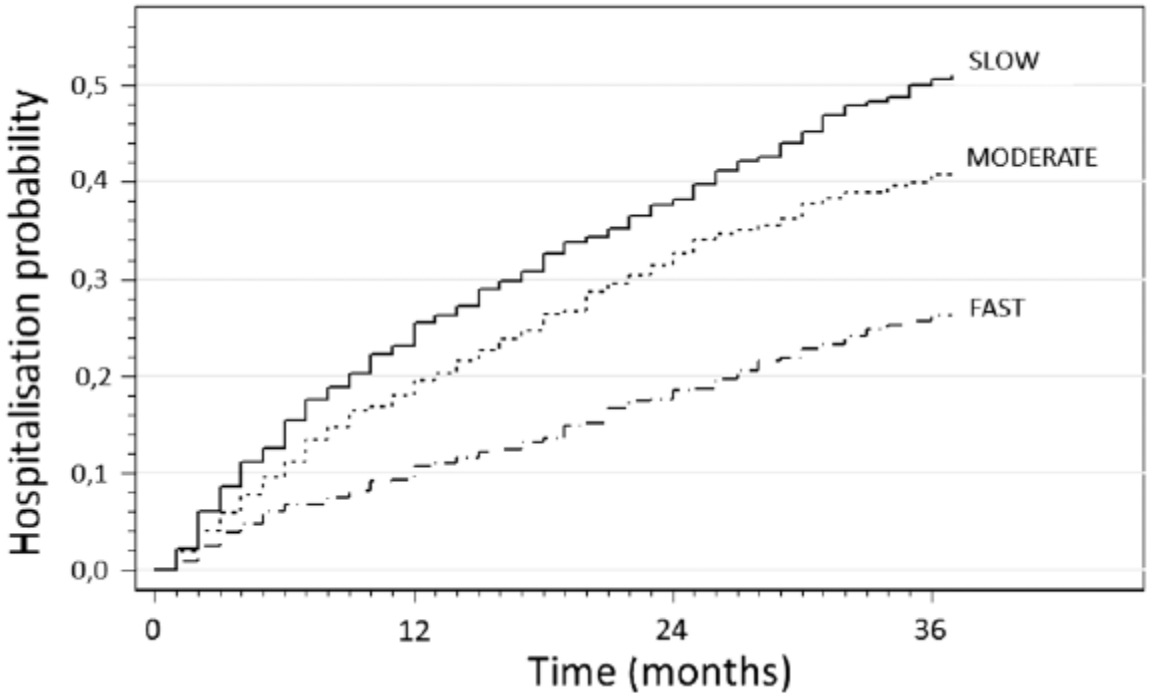
Full-adjusted relative risk of death from any cause according to quartiles of walking speed

Grazzi G. et al. *Int J Cardiol* 2014

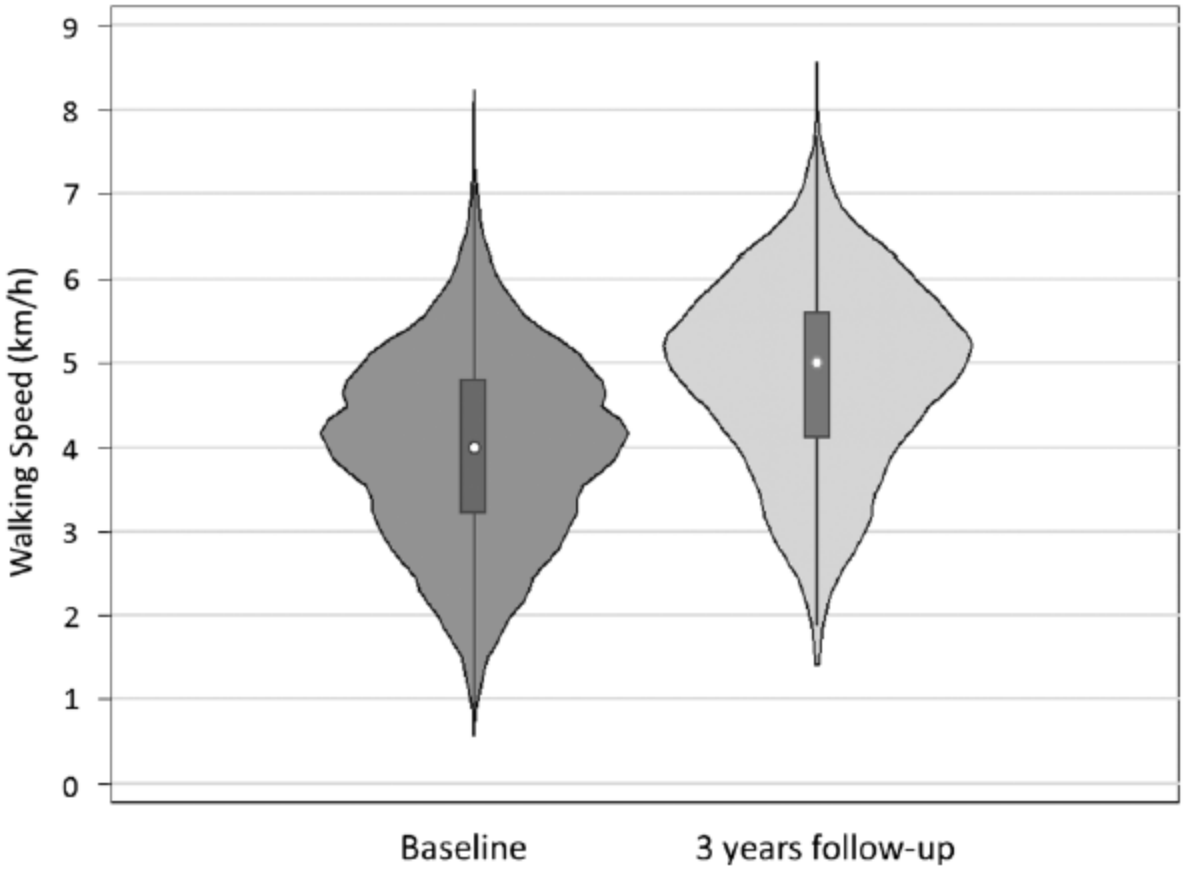
ORIGINAL ARTICLE

Improved walking speed is associated with lower hospitalisation rates in patients in an exercise-based secondary prevention programme

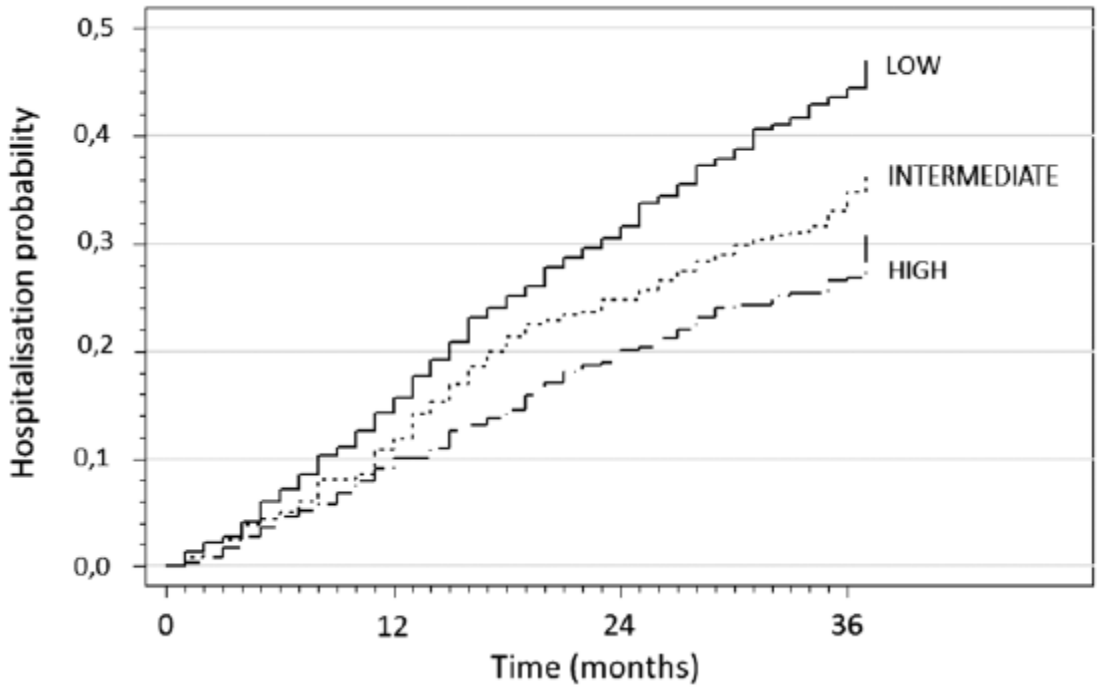
Grazzi G. et al. *Heart* 2016



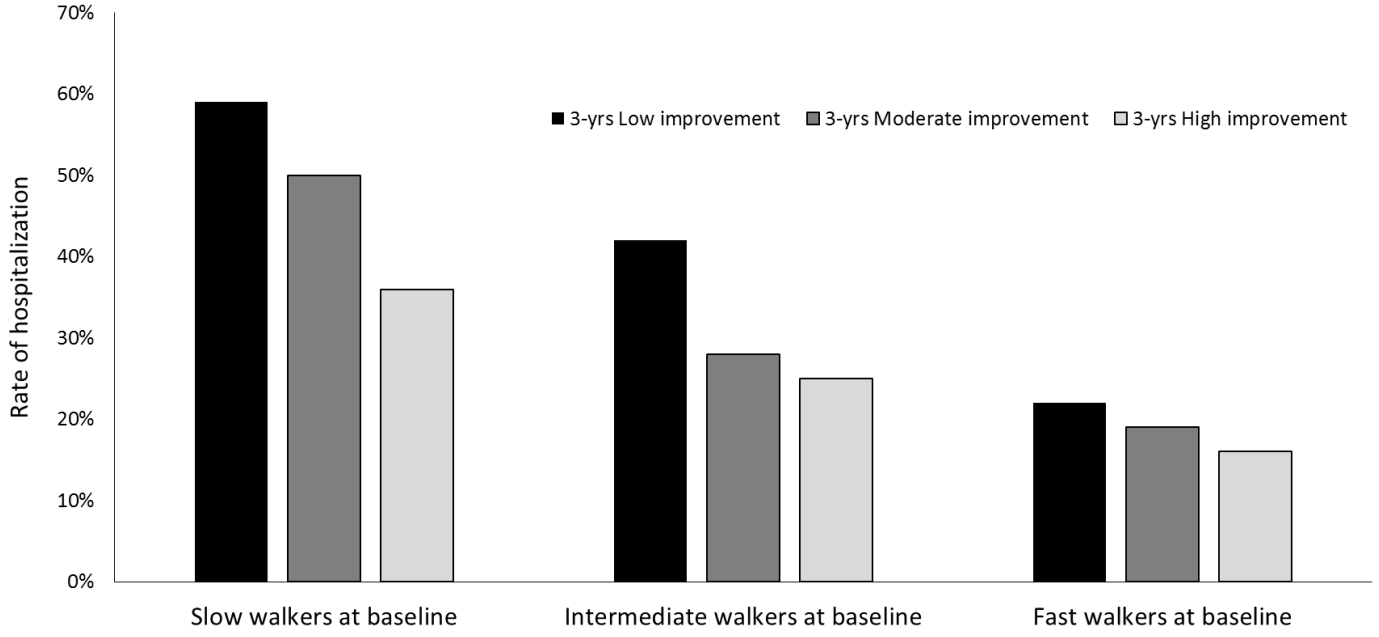
Grazzi G. et al. *Heart* 2016



Grazzi G. et al. *Heart* 2016

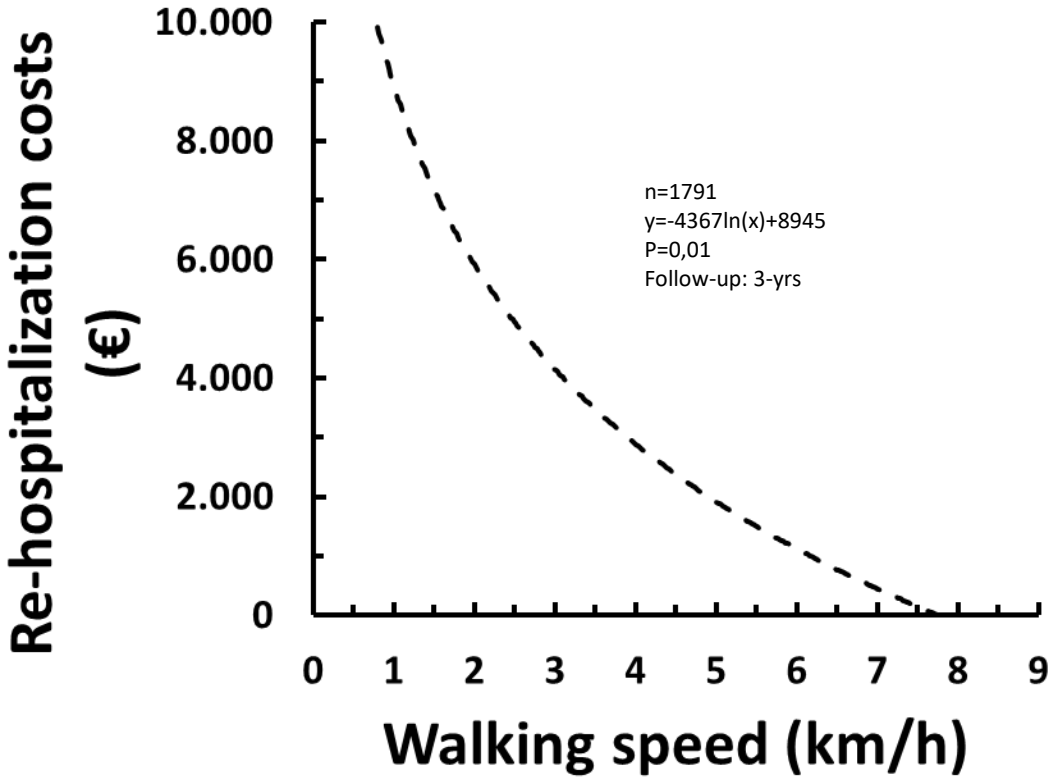


Grazzi G. et al. *Heart* 2016

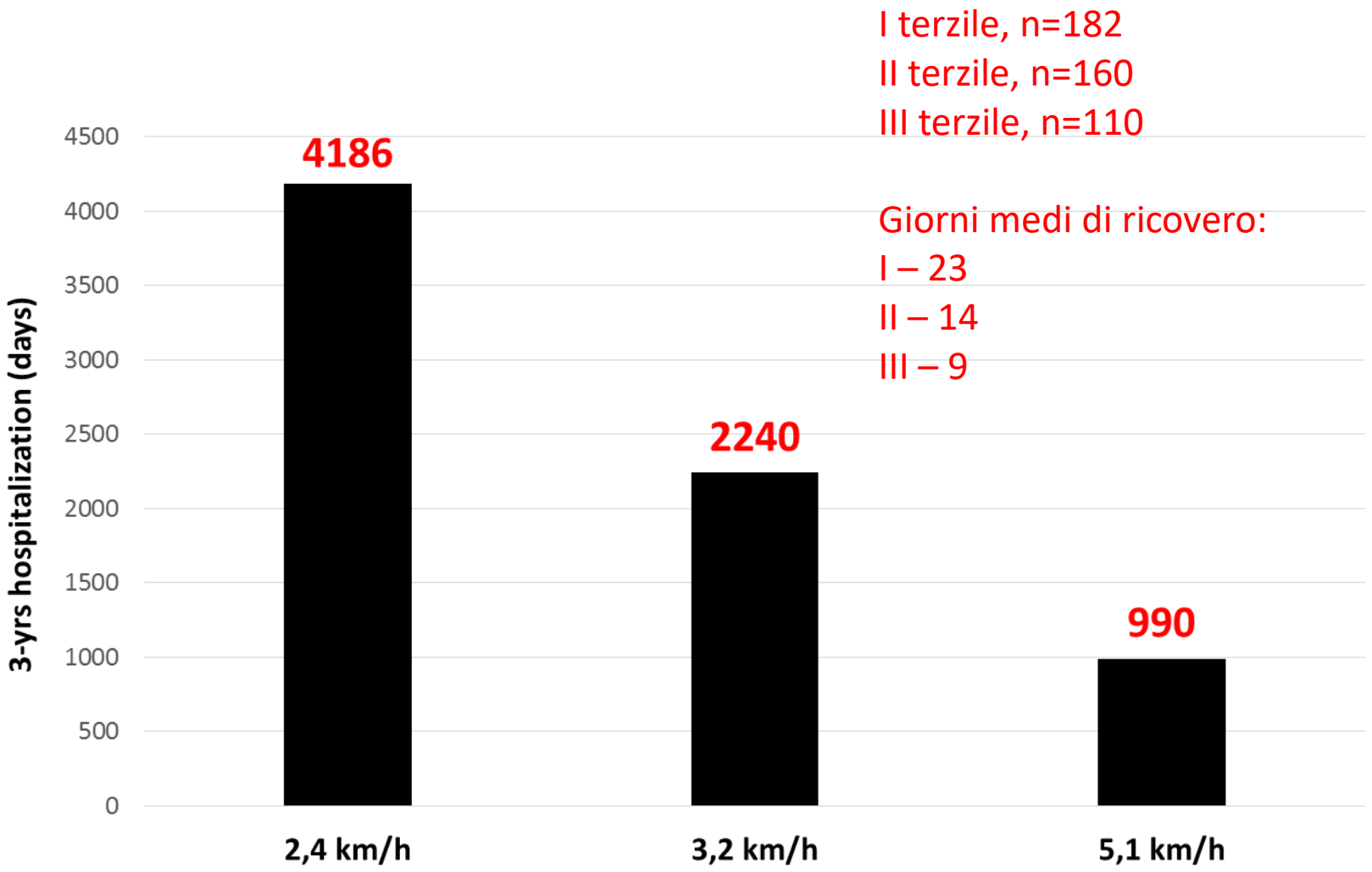


Grazzi G. et al. *Heart* 2016

Walking speed and costs for hospitalization

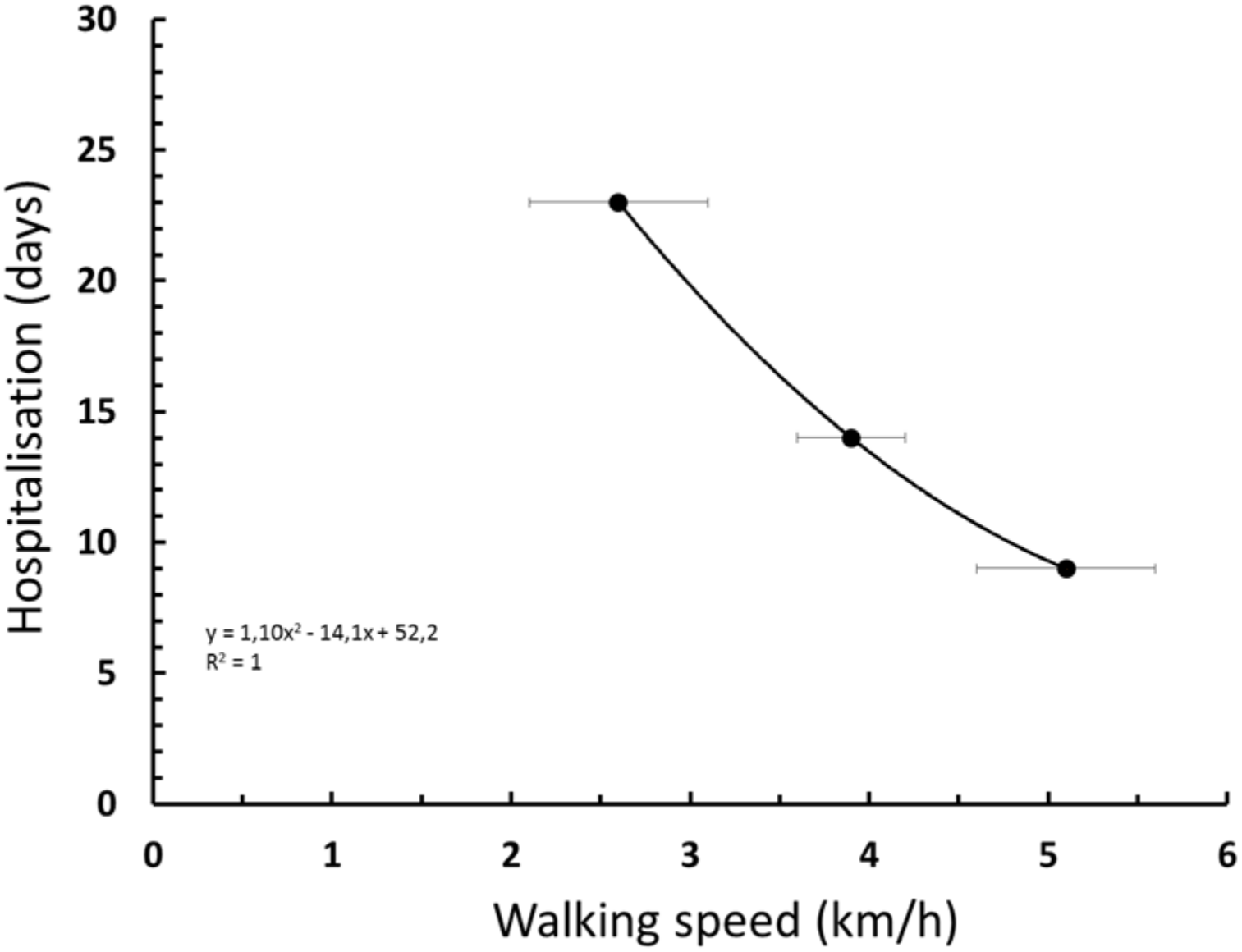


Grazzi G. et al, 2018, ahead of pub

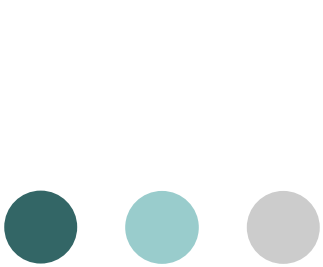


Analisi multivariata dopo trasformazione logaritmica significativa sia II v I, che III v I.

Merlo C. et al Europrevent 2018



Merlo C. et al Europrevent 2018



Part III

- Applicazione

Caratteristiche

Antropometriche	
Età (a.)	63 ± 10
Peso (kg)	86 ± 16
Altezza (cm)	170 ± 8
BMI	30 ± 6
Cliniche	
IMA rivascolarizzato	42
Rivascolarizzazione senza IMA	27
Altro	10
Fattori di rischio	
Famigliarità	48%
Ipertensione	77%
Dislipidemia	74%
Diabete	22%
Fumo	8%

(gruppo EFA-cardio FE/2013-1, n = 71)

	Pre*	Post*	P Value
Walking speed (km/h)	**4,2** ± 1,2	**5,0** ± 1,2	0,0001
HR (bpm)	90 ± 14	90 ± 13	ns
VO_2 peak (mL/kg/min)	22,1 ± 5,3	24,3 ± 5,2	<0.0001
Weekly training* (min)	28 ± 97	261 ± 119	<0.0001

* 2/sett EFA guidato-supervisionato
2/sett EFA guidato-in autonomia
Per 8-10 settimane

Criteri di Inclusione	Criteri di Esclusione
Firma del consenso informato	SC in classe NYHA III-IV
Ricovero per SCA	FE < 30%
Coronarografia ± PCI	Severa valvulopatia aortica o mitralica
Età ≥ 70 anni	Coronaropatia plurivasale o coinvolgimento del TC
Score SPPB 4-9 a T1	Lesione coronarica residua
	SPMSQ < 4
	Severa limitazione fisica all'esercizio
	Aspettativa di vita < 12 mesi

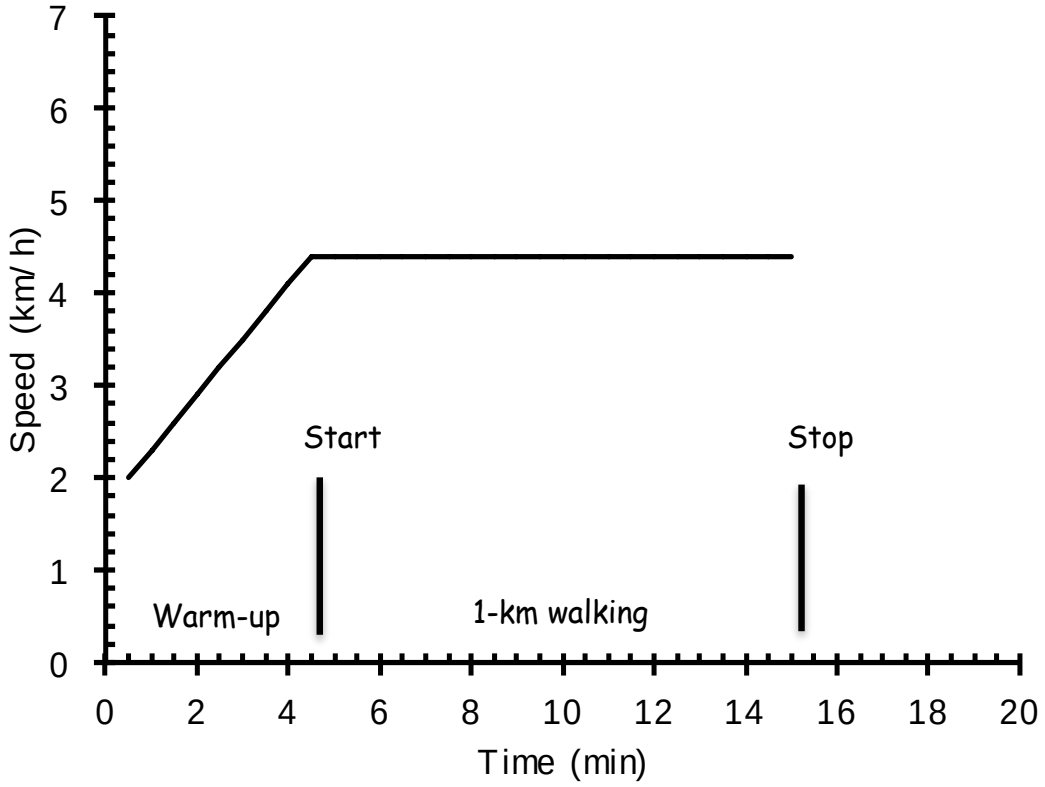
Caratteristiche dei soggetti esaminati	
n	46
Maschi/femmine (n)	36/10
Età	77,2 (4,6)
Peso (kg)	78,7 (12,9)
Altezza (m)	1,68 (0,09)
BMI (kg/m^2)	27,7 (3,7)
Fattori di rischio (n, %):	
Ipertensione	45 (98)
Dislipidemia	43 (93)
Sovrappeso/obesità	17/15 (37/33)
Diabete	10 (22)
Sedentarietà	29 (63)
Dieta sbilanciata	18 (39)
Fumo	29 (63)
Diagnosi (n, %):	
STEMI	14 (30)
NSTEMI	26 (57)
Angina instabile	6 (13)
Pregresso IMA (n, %)	14 (30)

Farmaci	Soggetti (n, %)
ASA	46 (100)
Clopidogrel	16 (35)
Ticagrelor	29 (63)
Prasugrel	1 (2)
Beta-bloccante	34 (74)
ACE-inibitore	31 (67)
Sartano	11 (24)
Statina	44 (96)
Calcio-antagonista	8 (17)
Diuretico	11 (24)
Ivabradina	0 (0)
Ranolazina	0 (0)

Short Physical Performance Battery

SPPB	
Equilibrio	Standing balance test
Forza muscolare	Standing chair test
Velocità di cammino breve	4m - Usual walking speed test
Performance fisica	Score finale

1km – Treadmill Walking Test



Valutazione funzionale di:

- FC media (bpm)
- FC massima (bpm)

- Velocità media (km/h)
- Velocità massima (km/h)

- VO_2peak (ml/kg/min)
- VO_2peak (%pred)

Chiaranda G. et al. *J Cardiopulm Rehabil Prev*, 2012

Esercizio Raccomandato

- CRF
  - Cammino
  - Intensità moderata (come 1k-TWT)
  - Almeno 30 minuti (anche 10x3)
  - Almeno 3/sett
- Forza/Equilibrio
  - Esercizi OTAGO
  - A partire dal 2° mese

SPPB

SPPB (n = 40)	T1	T4	Differenza	P
Standing balance	3,7 (0,6)	3,7 (0,7)	0 (0,1)	0,850
Usual walking speed	2,1 (0,8)	3,0 (0,9)	0,9 (0,1)	< 0,001
Standing chair	1,6 (0,8)	2,3 (1,2)	0,7 (0,1)	< 0,001
SPPB score	7,4 (1,2)	9,0 (2,0)	1,6 (0,4)	< 0,001

I dati sono presentati come media (± DS)

1k-TWT

1k-TWT (n = 33)	T1	T4	Differenza	P
Velocità media (km/h)	3,2 (1,2)	4,3 (1,2)	**1,1 (0)**	< 0,001
Velocità massima (km/h)	3,4 (1,1)	4,5 (1,2)	**1,1 (0,1)**	< 0,001
FC media (bpm)	87 (14)	88 (10)	1 (4)	0,688
FC massima (bpm)	99 (11)	100 (12)	1 (1)	0,402
VO_2peak (ml/kg/min)	17,8 (4,2)	21,1 (4,8)	**3,3 (0,6)**	< 0,001
VO_2peak ($\%_{PRED}$)	76 (17)	89 (17)	**13 (0)**	< 0,001

I dati sono presentati come media (± DS)

Attività fisica svolta

Attività fisica svolta settimanale	T1	T4
Tipo		
Nessuna (n)	20	0
Cammino (n)	11	30
Altro (n)	2	3
Intensità		
0/3 (n)	12	16
1/3 (n)	1	17
Durata		
Ore (media)	1,6	4,5
MET/h/sett (media ± DS)	**4,9 ± 7,4**	**15,8 ± 9,3**

Discussione

- *I risultati ottenuti sono* ***clinicamente rilevanti?***

SPPB

	Effect size method	
	Small change	Substantial change
SPPB score	0,28	**0,71**

Kwon S. et al. *J Nutr Health Aging*, 2009

SPPB

	Effect size method		
	Small change minimally significant	Substantial change	1k-TWT Study
SPPB score	0,28	0,71	1,6
400-MWT (sec)	20-30	50-60	288 (su 1000m)

400MWT: "as quickly as possible."
At the end of each lap (40-m), standard encouragement was given, as well as laps remaining (e.g., "4 down, 6 to go").

Kwon S. et al. *J Nutr Health Aging*, 2009

VO_2peak

	All-cause mortality reduction (+ 1 ml/kg/min)	Mode	n	Mean age	Follow-up
Kavanagh (2002)	**9%**	Bike CPX	12169	55	7,9
Keteyian (2008)	**15%**	Balke CPX	2018	61	4,9
Grazzi (2014)	**7%**	1k-TWT	1255	61	8,2

Kavanagh T. et al. *Circulation*, 2002.
Keteyian S.J. et al. *American Heart Journal*, 2008.
Grazzi G. et al. *International Journal of Cardiology*, 2014.

VO_2peak

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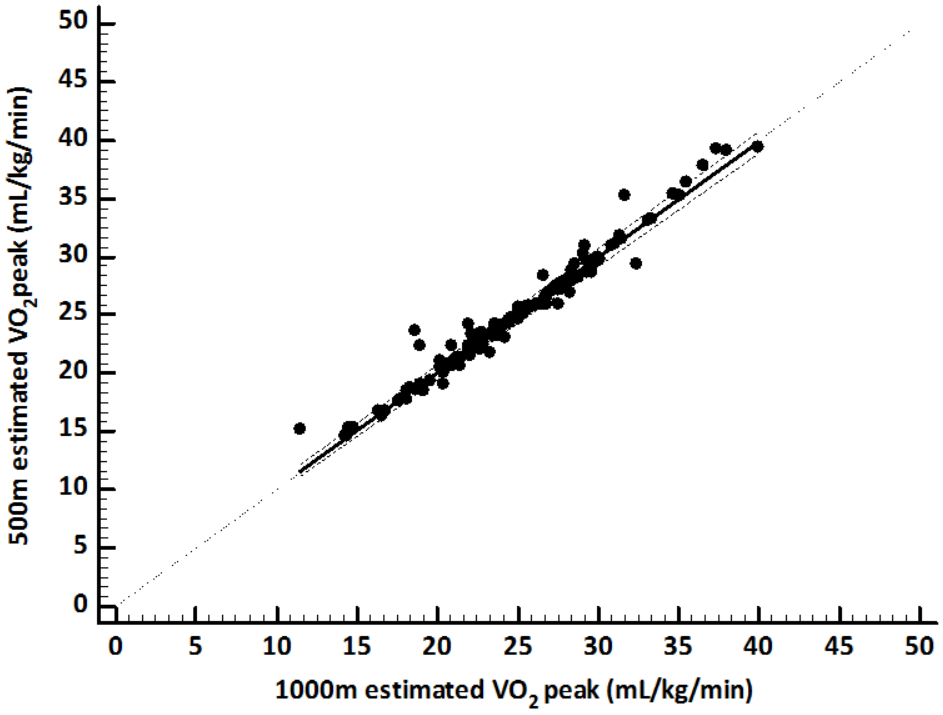
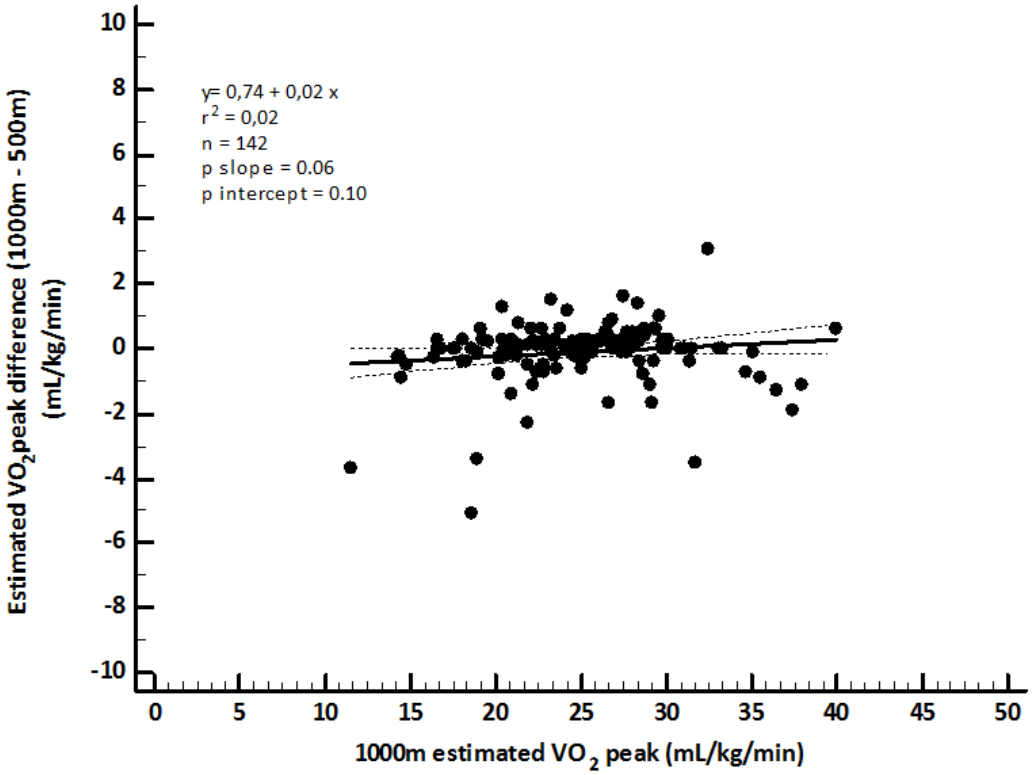
Grazzi (2014)	**7%**	1k-TWT	1255	61	8,2
1k-TWT Study (2018)	**(+3,3 ml/kg/min) Potenziale 23%**	1k-TWT	33	77	-

… bastano 500-m…



500-m vs 1000-m



… 100-m vs 1000-m…